ORIGINAL ARTICLE

PROGNOSTIC FACTORS OF LEPTOSPIROSIS PATIENTS IN DR. SARDJITO GENERAL HOSPITAL, YOGYAKARTA, INDONESIA

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ABSTRACT

Background: *Leptospirosis, an infectious disease that affects humans and animals, is a common zoonosis with a variety of clinical manifestations. Yogyakarta is one of the cities with a high incidence of leptospirosis. It is important to recognize the clinical features and prognostic factors of this disease. Severe disease can be fatal, although majority of cases are mild and self-limited.*

Objective: *To determine the prognostic factors for leptospirosis that associated with mortality in patients with leptospirosis in Dr. Sardjito General Hospital, Yogyakarta.*

Methods: *We conducted a retrospective study of data collected in our hospital between Jan 2010 until May 2011, from whom the diagnosis of leptospirosis was confirmed based on pertinent clinical and epidemiological data and positive serology.*

Result: *Thirty two patients were included in this study, including 29 survivors (90.62%) and 3 non-survivors (9.38%). Of these 32 patients, 26 patients (81.25%) were admitted to the medical ward and 6 patients (18.75 %) were admitted to the ICU. Multivariate logistic regression demonstrated that three factors were independently associated with mortality: higher level of potassium (OR 10.8; CI 1.194-97.728; p<0.01) on admission and neurological dysfunction (altered mentation or seizure) (OR 30; CI 4.367–206.07; p<0.01)*

Conclusion: *The mortality of leptospirosis remains high despite improvements in patients care. In order to improve the early treatment of high-risk patients, these higher levels of potassium on admission and neurological dysfunction, which are associated with mortality, can be used at the time of admission as prognostic factors.*

Keywords : *Leptospirosis, prognostic factors, mortality*

Background

Leptospirosis is the most widespread zoonosis with recent outbreaks in several Asian, Central, and South American countries.[1] Leptospirosis is a *zoonotic* disease, which is caused by *Leptospira* and transmitted to human by contact with *Leptospira* contaminated animal urine or *Leptospira* contaminated environment. Thirty-two patients with Leptospirosis had admitted in Dr. Sardjito General Hospital from January 2010 until May 2011.[2] In Indonesia, the spread of leptospirosis is in the Province of West Java, Central Java, Yogyakarta, Lampung, South Sumatra, Bengkulu, Riau, West Sumatra, North Sumatra, Bali, NTB, South Sulawesi, North Sulawesi, East Kalimantan and West Kalimantan. The mortality rate of leptospirosis in Indonesia is high, reaching 2.5 to 16.45%. At the age of over 50 years mortality rate can be up to 56%. When Leptospirosis patient is accompanied by a yellow lining of the eye indicating damage to liver tissue, the risk of death will be higher. Several publications reported mortality rates between 3% -54% depending on the infected organ system.[3]

We believe that early evaluation of disease severity at the time of admission might be useful in improving the care of patients with leptopsirosis.

Objective

The purpose of this study is to determine the prognostic factors for leptospirosis that associated with mortality in patients with leptospirosis at Dr. Sardjito Hospital, Yogyakarta.

Methods

Patient population. This study was performed in Dr. Sardjito General Hospital, Yogyakarta. All patients admitted over period January 2010 until May 2011 with suspected leptospirosis were retrospectively included in the study. Leptospirosis was defined in accordance with modified Feine's score criteria. Briefly, six clinical criteria (headache, fever, conjunctiva suffusion, meningeal signs, myalgia, and jaundice), two laboratory-determined criteria (albuminuria or azotemia), and epidemiological criterion (contact with rats or contaminated water) were scored. Leptospira was suspected when the score was ⩾ 20, with a strong presumption when the score was > 26. In every case, the diagnosis was later confirmed using IgM ELISA (Panbio, Australia) for leptospirosis. From the total of 39 patients tested, it was found that 32 patients were positive for IgM ELISA and were included in the final analysis. We did not identify the serogroups involved. [4,5]

When the diagnosis had been confirmed, the patients' medical records were reviewed. The demographic data (age, gender, and occupation) and epidemiological data (exposure and time between the onset of clinical signs and hospitalization) were collected.

Clinical definitions. From the clinical data collected, there were presence of jaundice, fever (temperature ⩾ 38.5°C), and dyspnea (respiratory rate > 20). Organ dysfunction was defined as: (a) Neurological: presence of seizures or altered sensorium; (b) Respiratory: abnormal chest x-ray, clinical evidence of pneumonia or pleural effusion; (c) Cardiac: evidence of cardiac failure, S3 or EKG changes : rhythm abnormalities (sinus tachycardia [> 120 bpm], bradycardia [< 50 bpm], atrial or ventricular extra-systoles, and atrial fibrillation), repolarization abnormalities (T wave inversion, abnormal positive T wave, and depression of the ST segment), or conduction abnormalities (right or left branch block, left anterior hemiblock, and atrioventricular block); (d) Renal: oliguria (<0.5 L/24 hours) or serum creatinine >3 mg/dL; (e) Hepatic: serum bilirubin >10 mg/dL and elevated hepatic enzymes, hepatic encephalopathy; (f) Bleeding: petechiae/purpura, hemetemesis, hemoptysis, epistaxis, or melena.

Outcome. The patients were observed until they completely recovered and discharged from the hospital or until they died. The cause of death was registered in every case, but no postmortem examinations were performed. [4,5]

Statistical Methods. Results are expressed as means ± SD or as percentages. Clinical and laboratory data were statistically analyzed with the use of the χ^2 tests or Fisher's exact test for the comparison of proportions and analysis of variance for the comparison of intergroup difference. Risk factors for death were identified with the use of the χ^2 statistic for the differences in the distribution of categorical variables between survivors and non-survivors. Variables found to be relevant and associated with death ($p < 0.05$) were entered in a multiple logistic regression model (SPSS software for Windows). Adjusted odds ratios and 95% confidence intervals were calculated. A value of $p < 0.05$ was considered significant. [6,7]

Result

Thirty-two patients met the inclusion criteria, including 29 survivors (90, 62%) and 3 non-survivors (9.38%). Of these 32 patients, 26 patients (81.25%) were admitted to the medical ward and 6 patients (18.75 %) were admitted to the ICU. The 3 non-survivors all died in medical ward. All death was attributed to irreversible septic shock. The mean hospital stay ± SD for the survivors was 10.4 days ± 4.2 days. Demographic data are presented in Table 1.

Table 1. The mean hospital stay ± SD for the survivors

Variabel	Survivors	Non-survivors	p
Gender, n (%)			
Man	21	3	
Woman	8	0	0.55
Age (years), mean ± SD	42.41 ± 13.44	57.33 ± 14.43	0.2
20-46 years	17	0	
47-76 years	12	3	0.092
At risk occupation, n (%)			
Yes	12	2	
No	17	1	0.57
Rodent exposure, n (%)			
Yes	21	2	
No	8	1	1
Hemodialisis, n			
Yes	10	1	
No	19	2	1
ICU, n			
Yes	4	2	
No	25	1	0.083

The mean age ± SD for the survivors was 42.41 years ± 13.44 years, and for the non-survivors was 57.33 years ± 14.43 years. In age variable there was no differences between the survivors and non survivors (p = 0.092)

The gender ratio between male and female patients with leptospirosis was 3:1, man 75% and women 25%. There was no differences in gender between the survivors and non survivors (p = 0.55)

Table 2. Clinical sign and symptoms in survivors and non survivors among patients with Leptospirosis

Sign and symptoms	Survivors (n = 29)	Non survivors (n = 3)	p value
Fever	2	0	1.000
Dyspnea	15	2	1.000
Jaundice	19	3	0.534
Cardiovascular collapse	16	1	0.589
Conjunctival Suffusion	21	2	1.000
Oliguria	9	3	0.044*
Respiratory symptoms	7	2	0.184
Neurological dysfunction	0	2	0.006*
Hemorragic	1	1	0.181

*statistically significant

Table 3. Result of univariate analysis of laboratory values between survivors and non-survivors among patients with leptospirosis.

Value	Survivors (n = 29)	Nonsurvivors (n = 3)	p
Urea nitrogen (mg/dL)	79.12 ± 43.14	139 ± 6.56	0.000*
Creatinine (mg/dL)	6.17 ± 3.32	8.43 ± 3.75	0.275
Total protein (g/L)	5. 71 ± 0.69	5.6 ± 0.21	0.793
Albumin (g/L)	2.11 ± 0.46	1.61 ± 0.27	0.081
Total Bilirubun (mmol/L)	7.76 ± 8.59	14.48 ± 4.78	0.099
Sodium (mmol/L)	125.9 ± 9.67	144.2 ± 15.77	0.027
Potassium (mmol/L)	4.05 ± 0.81	5.29 ± 1.08	0.02*
Chloride (mmol/L)	93.98 ± 10.23	100 ± 15.62	0.359
Uric (mg/dL)	9.46 ± 3.66	11.5 ± 2.95	0.286
AST (IU/L)	71 ± 46.2	123 ± 110.59	0.365
ALT (IU/L)	53.58 ± 24.38	84.67 ± 48.44	0.064
Glucose (mg/dL)	132.17 ± 72.02	115 ± 33.41	0.628
WBC count (10^9/L)	14.39 ± 5.29	13.74 ± 2.53	0.837
Platelet count (10^9/L)	115.41 ± 87.05	76.67 ± 84.51	0.301
Hemoglobin (g/L)	11.84 ± 1.54	11.5 ± 0.26	0.305
Hematocrit (%)	33.19 ± 4.59	32.5 ± 1.9	0.651

*statistically significant

Table 4. Result of multivariate stepwise logistic regression analysis of risk factors for patients with Leptospirosis.

Risk Factor	OR	95% CI	P value
Oliguria	0.75	0.541 – 1.04	0.018
Urea nitrogen (mg/dL)	0.813	0.642 - 1.028	0.025
Potassium (mmol/L)	10.8	1.194 – 97.728	0.009
Neurological symptoms	30	4.367 – 206.07	0.000

Discussion

In this study, several poor prognostic factors in leptospirosis have been identified, including higher admission serum potassium and neurological dysfunction (altered mentation or seizures) were associated with high in-hospital fatality.[8] In another retrospective study, advanced age, oliguria, cardiac arrhythmia, dyspnea, and pulmonary rales were associated with mortality.[9]

Mortality in leptospirosis ranges from 1% to 20 %. [1, 10, 11] In South India, a mortality of 5.32% was reported from Kolenchery and 3.5% from Madras. The study showed that there was no difference in mortality when patients were grouped by age, gender, at-risk occupation, or rodent exposure.

ARF occurs in 16% to 40% of leptospirosis and approximately 30% to 50% are non-oliguric,

with a worse prognosis for oliguric renal failure.[10] Ninety-seven percent of the patients had renal failure and all patients who died were oliguric. In our study, oliguria was a very sensitive criterion of the severity of the disease. Similarly, Seguro et al noted that the mortality rate for oliguric patients with acute renal failure were higher than that for patients with persistent dieresis. Again, 90% of leptospirosis is anicteric with a lower mortality compared with icteric forms. In our group, 68% of patients were icteric and there was no difference in mortality.

Neurologic dysfunction (altered mentation or seizures) was the most significant predictor of mortality; most patients with neurologic dysfunction also had significant renal and hepatic disease contributing to encephalopathy. Altered mental status was the strongest independent predictor of death in urban leptospirosis in Brazil; other poor prognostic factors were oliguria, advanced age, renal and respiratory insufficiency. In this study, there was an association between altered mental status and mortality.[12]

Conclusions

The mortality of leptospirosis remains high despite improvements in patients care. In order to improve the early treatment of high-risk patients, these two clinically and two laboratory criteria, independently associated with mortality, could be used at the time of admission.

References

1. Vinetz JM. Leptospirosis. *Curr Opin Infect Dis*. **2001**; 14:527–538.
2. Tunissea A. Anlisis Spasial Faktor Risiko Lingkungan pada Kejadian Leptospirosis di Kota Semarang. **2008;** 1-4.
3. Murtiningsih B, Budiharta S, Supardi S. Faktor Risiko Leptospirosis di Provinsi Yogyakarta dan sekitarnya. **2005**; BKM; 21:1-8.
4. Dupont H, Perdrizet DD, Perie JL, et al. Leptospirosis: Prognostic Factors Associated with Mortality. *Clinical Infectious Diseases* **1997**; 25:720–4.
5. Unnikrishnan D, Pisharody R, Vijayalakshmy N. Prognostic Factors in Leptospirosis. A study from Kerala, India. *Infectious Diseases in Clinical Practice* **2005;** 13:104-107.
6. Riwidikno H. Uji Beda. In Statistik Kesehatan : Belajar mudah teknik analisis data dalam Penelitian Kesehatan. Jogjakarta: Mitra Cendikia Press. **2007**; 4-70.
7. Dahlan, M. Sopiyudin. Uji Hipotesis. In statistika untuk Kedokteran dan Kesehatan. Jakarta : PT. Arkans. **2006**; 1-135.
8. Lopes AA, Costa E, Costa YA, et al. The association between serum potassium at hospital admission and the case-fatality rate of leptospirosis in men. *Rev Inst Med Trop Sao Paulo*. **2001**; 43:217–220.
9. Daher E, Zanetta DM, Cavalcante MB, et al. Risk factors for death and changing patterns in leptospirosis acute renal failure. *Am J Trop Med Hyg*. **1999**; 61:630–634
10. Levett PN. Leptospirosis. *Clin Microbiol Rev*. **2001**;14:296–326
11. Muthusethupathi MA, Shivakumar S, Vijayakumar R, et al. Renal involvement in leptospirosis—our experience in Madras City. *J Postgrad Med*. **1994**; 40:127–131.
12. Ko AI, Galvao Reis M, Ribeiro Dourado CM, et al. Urban epidemic of severe leptospirosis in Brazil. Salvador Leptospirosis Study Group. *Lancet*. **1999**;354:820–825